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EXAMINER				
WOITACH, JOSEPH T				
ART UNIT		PAPER NUMBER		
1632				

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/844,705

Applicant(s)

BOSWORTH ET AL.

Examiner

Joseph T. Woltach

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- IF NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 06 January 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 3-6 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 3-6 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

### DETAILED ACTION

This application filed April 27, 2001 is a continuation of 09/443,766 filed November 19, 1999, which claims benefit under 35 U.S.C. 120 to PCT/US98/10318, filed May 20, 1998, which claims benefit to provisional application 60/047,181, filed May 20, 1997.

Applicants' amendment filed January 6, 2004, has been received and entered. Claims 3-5 have been amended. Claims 3-6 are pending and currently under examination.

### *Claims*

Claims 3-5 objected to because of the following informalities: the claims recite "ECF18R" is withdrawn.

As noted in Applicants amendment, page 7, section VIII, the claims have been amended to spell out *E. coli* F18 receptor. The amendments to the claims has obviated the basis of the objection.

### *Claim Rejections - 35 U.S.C. § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Newly amended claims 3-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

Art Unit: 1632

application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application". Specifically, the claims have been amended to recite "binding to the *E. coli* F18 receptor (ECF18R) in swine", however this limitation is not supported by the specification. The support pointed to by Applicants does not specifically provide support for the new amendment. A review of the present specification indicates that (ECF18R) is a candidate gene representing the *E. coli* F18 gene locus, not simply a F18 receptor (see page 2, line 4 or page 8, line 7). This was also noted in the basis of the rejection made under 35 USC 112, second paragraph, in the previous office action (see top of page 8, paper number 10). Further, an *E. coli* F18 receptor is not found in swine, it is an *E. coli* protein. Moreover, the polymorphism in swine described in the instant specification is in the FUT1 gene, and the colonization and potentially binding of *E. coli* is associated with this gene in the swine. Finally, it is noted that even if the claims were amended to recite the *E. coli* F18 gene locus the *E. coli* do not bind a locus or any gene in that locus, rather they bind the protein expressed from that locus, in this case Fut 1.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claims 3-5 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen,

650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure".

Claims 3-5 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying swine which are resistant to *E. coli* strain F18 associated intestinal disorders, said method comprising: a) providing a biological sample from a swine; b) determining the polynucleotide at position 307 of the open reading of alpha (1,2) fucosyltransferase gene (FUT1)(SEQ ID NO: 12), whereby the identification of an adenine at said position on both alleles of the swine is associated with swine which are resistant to *E. coli* strain F18 colonization; and c) identifying swine with an adenine at position 307 of the open reading of FUT1 gene as resistant to *E. coli* strain F18 associated intestinal disorders, and methods of using said identified swine for breeding, does not reasonably provide enablement for identifying an adenine at other positions within the FUT1 gene or for intestinal disorders associated with other *E. coli* strains.

Applicants note that the claims do not encompass identification of any adenine at other positions, only at position 307 of the FUT1 gene (see page 4, Section III). Further, Applicants note that the claims are not directed to any *E. coli* strain, only strains that can bind the *E. coli* F18 receptor (see bridging pages 6-7, Section VII). Applicants arguments have been fully considered, and found persuasive in part.

Initially, the amendments to the claims to provide a specific SEQ ID NO for the FUT1 gene encompassed by the claims provides a clear indication of the position of the polymorphism associated with the binding of *E. coli*. Has obviated the basis of the rejection as it is drawn to the specific identification of adenine within the FUT1 gene.

With regard to the breadth of any *E. coli* the amendments to the claims to encompass *E. coli* that bind "to the *E. coli* F18 receptor" appears to have attempted to narrow the claims to encompass only the *E. coli* that would bind and colonize the intestine of a swine as it is associated with the polymorphism of the FUT1 gene described in the instant specification. In the instant case, Applicants have shown a correlation with the presence of a homozygous polymorphism at base 307 in the open reading frame of the FUT1 gene and a resistance to *E. coli* strain F18 and thus, absence of the associated intestinal disorders. However, the mechanism of this resistance is not known nor described. As noted previously, even to date as evidenced in post filing art, Merjerink *et al.* (Mammalian Genomics 8:736-741) clearly indicates that the mechanism of the resistance was unknown at the time of the claimed invention (summarized in final sentence of abstract). Therefore, at the time of the invention made, the observation of the polymorphism associated with F18 resistance represents only a correlative analysis linking a specific phenotype with a specific genetic polymorphism and would not be extended to a

physical or functional reason for the resistance to intestinal disorders associated with *E. coli* colonization nor other strains of *E. coli*.

The specification teaches that it was observed that certain swine were naturally resistant to intestinal disorders associated with F18 *E. coli*. Furthermore, at the time of filing as exemplified by Merjerink *et al.* and Vogeli *et al.* and supported by the specification it has been demonstrated that the presence of the homozygous FUT1 allele represented by an adenine at position 307 of the open reading of FUT1 is associated with resistance to *E. coli* strain F18 associated intestinal disorders. The specification provides only this single specific alteration in the FUT1 allele and its association with only *E. coli* strain F18. It may be that other strains of *E. coli* strains can cause intestinal disease associated with colonization, however as noted by Bertin *et al.* and Duchet-Suchaux *et al.*, resistance of a swine to one strain of *E. coli* does not indicate resistance to other strains of *E. coli*. Thus, the presence of resistance to one strain of *E. coli*, is not, *a priori*, predictive of resistance to other strains of *E. coli*. As noted above, in this case the basis for the observed resistance in swine associated with the specific alteration in the FUT1 allele is not known, and absent evidence that the polymorphism results in a mechanistic reason for the resulting resistance, a genetic marker/polymorphism is simply a marker which can be associated with a specific characteristic. For example, the specification defines several other polymorphism in coding regions of the FUT1 and FUT2 genes, however none of these polymorphism are associated with any resistance to *E. coli* or any other observable phenotype. Moreover, the specification fails to detail that any other polymorphisms exist that are in linkage disequilibrium and can associated with the claimed method. There is no evidence that a polymorphism itself results in the phenotype, therefore the adenine at position 307 of the open

reading of FUT1 gene represents only a marker for the phenotypic observation of a swine resistance to F18 *E. coli*.

The amendment to the claims attempting to more narrowly define the types of *E. coli* that bind to the ECF18R and Applicants' arguments have not been found persuasive because there is no nexus between the observed genetic polymorphism and any functional characteristic of binding even for the strain of *E. coli* F18. The FUT1 gene encodes a glycosyltransferase that glycosylates a variety proteins in a subject providing for the H antigen (see specification page 3, lines 12-29). As supported by the prior art, it is proposed that the binding of *E. coli* in the intestine is due to the carbohydrate structure associated with the expression and activity of the Fut1. In this case, *E. coli* and other bacteria do not bind to the glycosyltransferases themselves, rather the bind to the carbohydrate structures generated by these enzymes. Narrowing the claims to encompass *E. coli* that bind a ECR18R (locus), or even one of the gene products like the FUT1 found at that locus is not found persuasive because there is no nexus with a genetic polymorphism and a specific functional characteristic with the gene or the gene product.

In view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time of the claimed invention was made, it would have required one of skill in the art undue experimentation to practice the invention as claimed, and therefore, the rejection is maintained.

***Claim Rejections - 35 U.S.C. § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:



Art Unit: 1632

A person shall be entitled to a patent unless --

(f) he did not himself invent the subject matter sought to be patented.

Claims 3-6 rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter is withdrawn.

Applicants note the declarations signed by the inventors and Applicants argue that there is no evidence that the instantly named inventors are not the inventors of the claimed invention. See Applicants' amendment, page 4-5, Section V.

Though the claimed inventions are similar, Examiner agrees that there is no objective evidence that the indicated inventors are not correct. Though each method requires that analysis of adenine at position 307 of the FUT1 gene, '859 uses this observation to provide a specific feed supplement, while the instant claims associates the polymorphism specifically with colonization. Though observed genetic polymorphism is the same in each case, the associated characteristic is different and thus can be observed by different inventors. In view of Applicants statements that the inventors of the claimed invention are correct, the rejection is withdrawn.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 3 and 4 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,355,859. Although the conflicting claims are not identical, they are not patentably distinct from each other.

Applicants argue that the claimed inventions are different noting that the instant method is drawn simply to identifying swine that are resistant to *E. coli* colonization, and the method of '859 to a method of improving weight gain. It is argued that the claimed inventions are directed to two different problems. See Applicants' amendment, page 6, Section VI. Applicants arguments have been fully considered, but not found persuasive.

The instant application and US Patent 6,355,859 share one common inventor and no common assignee. As noted by Applicants, that the priority documents have a common assignee, however the instant application does not share a common assignee as set forth in the previous office action (Applicants' amendment page 5, Section V, section b). Examiner would agree that in the instant application the claims are drawn to a method for identifying a swine that is resistant to intestinal colonization to a of strain of *E. coli* associated intestinal disorders by determining whether base pair 307 of the open reading frame of FUT1 is an adenine, and in particular the *E. coli* is strain F18. In the '859 patent the claims are drawn to a method for controlling weight in a swine by determining whether a swine is genetically resistant to F18 *E. coli* colonization by determining base pair 307 of the open reading frame of FUT1 is an adenine. Initially, in each case the claims require practicing the analysis of the FUT1 gene at position 307.

Moreover, it is well known in the art that colonization of specific strains of *E. coli*, such as F18, result in severe diarrhea and result in weight loss. Practicing the first method step of the methods of '859 would anticipate the instantly claimed methods. In addition, the method encompassed by claims 3 and 4 in the instant application results in identifying a swine which is resistant to F18 *E. coli* colonization and the resulting symptoms associated with said colonization and therefore, would make obvious the identification a swine capable of more controlled weight gain in a herd generally susceptible to F18 *E. coli* colonization. Practicing the method encompassed by claims 3 and 4 of the instant specification would anticipate the method and results accomplished in claims 1 and 4 in '859.

Claims 3-6 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,596,923. Although the conflicting claims are not identical, they are not patentably distinct from each other.

Applicants note that they do not agree with the basis of the rejection, but note that they are willing to file a terminal disclaimer if claims are allowed.

Applicants indication of filing a terminal disclaimer is noted, however no claims have been found allowable. A rejection can not be held in abeyance. Because Applicants have not provided any specific arguments in traverse of the rejection, the rejection is maintained for the reasons of record. As set forth in the previous office action, the method of '923 would anticipate the instantly claimed methods set forth in claims 3 and 4 because in each case a alteration/mutation if the FUT1 gene is being identified. Moreover, the mutation/alteration in the FUT1 gene is associated with decreased intestinal disorders. Claim 5 comprises practicing the

Art Unit: 1632

methods set forth in claims 3 and 4 and provides an additional step of mating the identified swine for the implicit intention of obtaining additional or more pure bread swine with the particular genotype that is associated with the desired phenotype of being more resistant to intestinal disorders associated with *E. coli*. Claim 6 specifically sets forth that the *E. coli* is strain F18, which is specifically set forth in claim 1 of '923. Claims 5 and 6 are included in this rejection because they would be considered an obvious step of practicing the method set forth in claim 1 (also of claims 3 and 4) as set forth in step (a) of claim 5.

### ***Conclusion***

No claim is allowed.

As indicated in the previous office action, the claims are free of the art of record. The art indicates that cell surface receptors on intestinal cells are the target molecules for *E. coli* colonization, and that the glycosylation on said receptors may be important in determining the ability of a particular *E. coli* to colonize the intestine. However, the art fails to specifically teach that an adenine at position 307 of the open reading frame of alpha (1,2) fucosyltransferase (FUT1) (SEQ ID NO: 12) can be correlated with resistance to *E. coli* strain F18 and possibly with the subsequent associated diseases.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

Art Unit: 1632


MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (571) 272-0734.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach



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